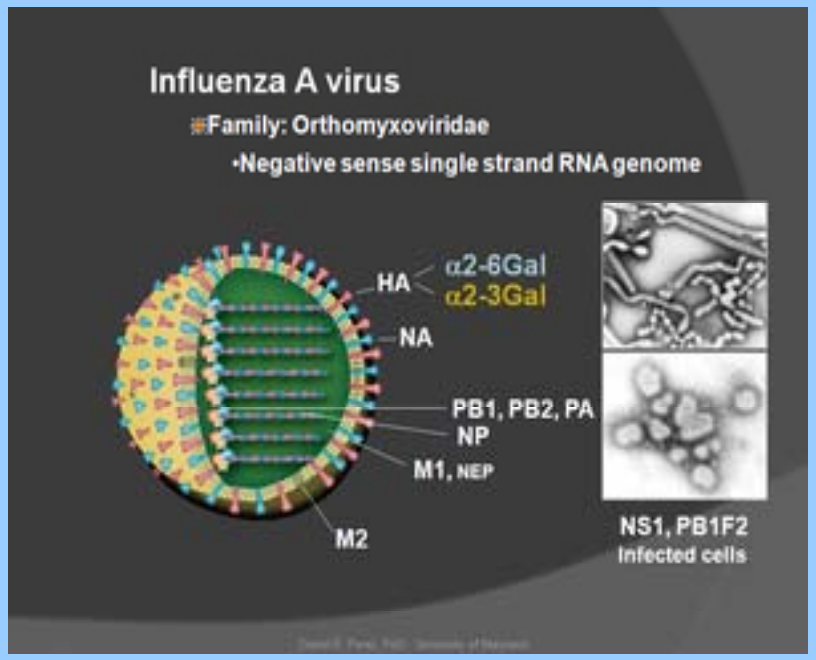
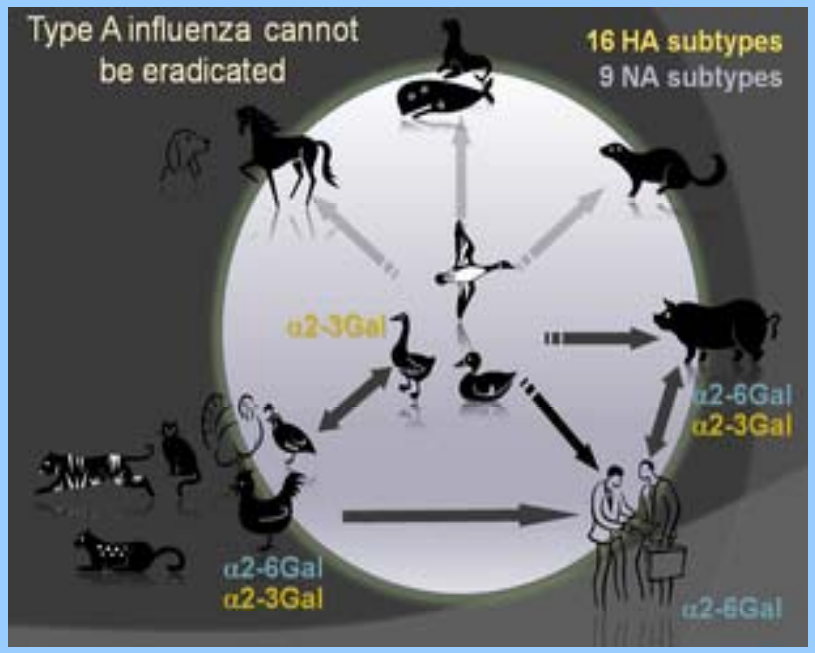
# H1N1: An Overview

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**Chief Physician, Health Systems**
**MITRE Corporation**

# Report Documentation Page

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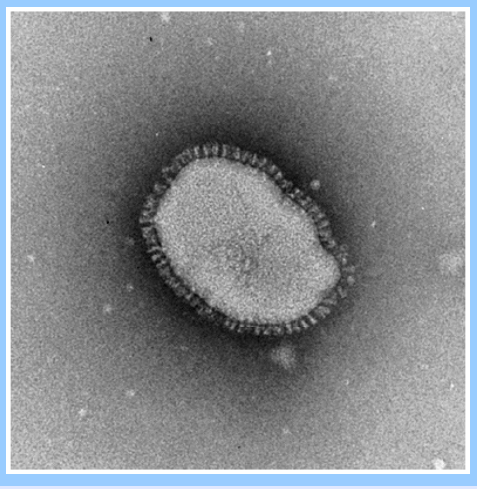
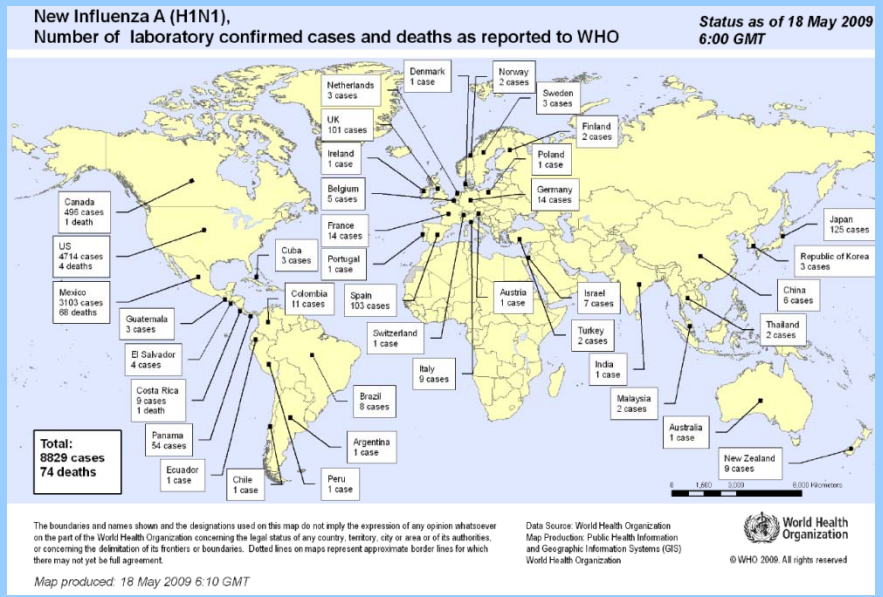
# Overview

- **Introduction, ROE, Disclaimers, Acknowledgements**
- **The Human Health Story**
- **The Agent: Influenza A**
- **The Disease: "You and Me"**
  - » **Clinical Medicine**
- **The Epidemic: "The Herd"**
  - » **Population Health**
- **Prevention, Preparation and Mitigation**
  - » **Seasonal Influenza**
  - » **Pandemic Influenza**



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# Introduction, ROE, Disclaimers, Acknowledgements

Goals:

- A broad appreciation of the medical, biological, epidemiological and public health challenges in managing seasonal influenza and pandemics
- Emphasize some practical individual health strategies and planning that may protect employees and their families during the fall influenza season and beyond

ROE:

- Questions at anytime

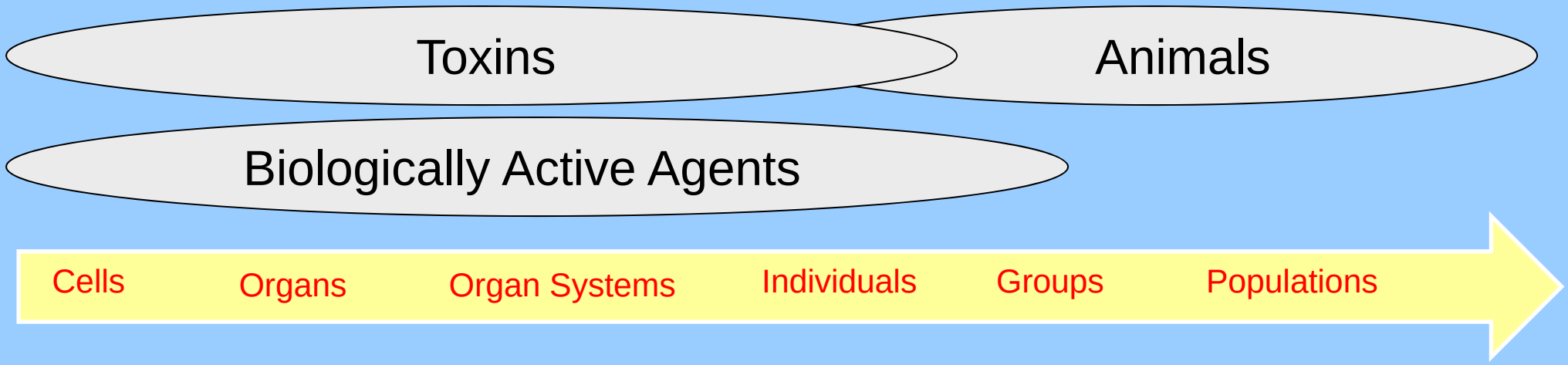
Disclaimers:

- Individual medical advice = Your primary care advisor
- MITRE Health Services, Business Continuity Program Office

Acknowledgements:

- NEJM, May 7, 2009, multiple articles (Triple Reassortment, Novel H1N1)
- Dori Reissman, MD, MPH; CDC
- Jean Otto, DrPH: Armed Forces Health Surveillance Center
- David Siegrist, PhD; Lynn Cooper, PhD; MITRE

# The Human Health Story




The Agent:
Microbiology/Pathology

The Disease:
Clinical Medicine

The Epidemic:
Epidemiology & Population Health

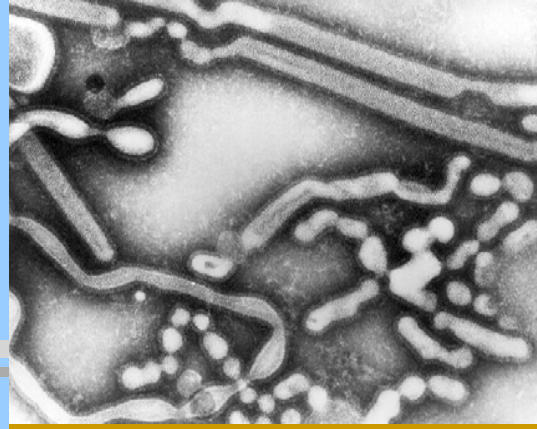
Anthropology/Public Health

Psychology

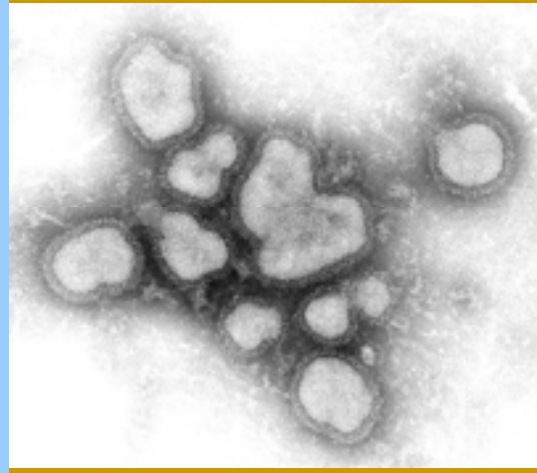
Anatomy & Physiology/Medicine

# The Agent: Influenza A

- Influenza, also know as Flu, is a respiratory disease caused by the influenza A, B or C virus.
  - » Virus: obligate parasite, not “alive” and must “invade” a host, RNA/DNA strands
- Flu is contagious (H1N1: RNA Polymerase—PB2) and can be a mild, severe or, at times, deadly disease.
- In most hosts, the viral point of entry is the upper respiratory tract (nose, throat) and the primary target is the columnar epithelium of the airway (trachea, bronchi, bronchioles), H1N1: Alpha 2-6 Glycan Receptors.
- Epidemiology (Seasonal Flu):
  - » Between 5-20% of the U.S. population each year
  - » 200,000 hospitalizations
  - » 36,000 US deaths and 250,000 Global deaths



Transmission Electron Micrograph of influenza A virus



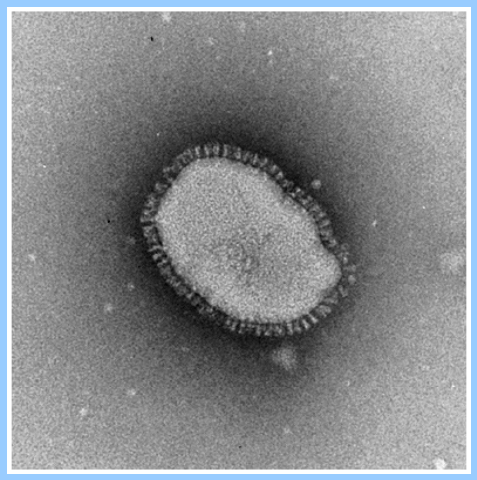
Negative stain of the influenza virus

Source: CDC

# The Agent: Influenza A

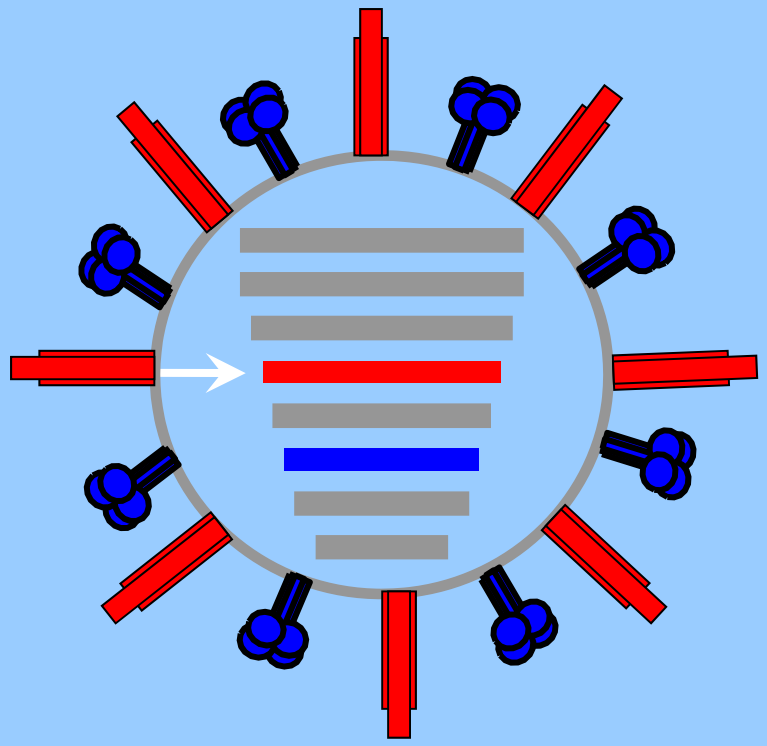
Entry Key: HA, Receptor Binding Site

Hemaglutinin

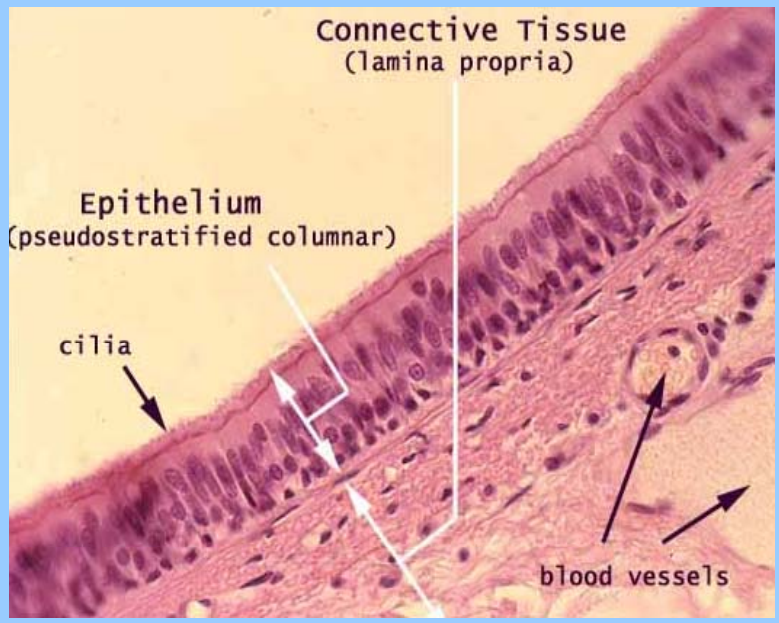


Exit Key: NA

Neuraminidase



8 Gene Segments




Circulating Human Strains

H3N2 since 1968
H1N1 (human) since 1977
H1N1 (swine) ? 2009



Source: Dr. Juan Arroyo, MITRE

# The Agent: Influenza A & Viral Diversity

- There are 16 distinct HA* types and 9 distinct NA types; all are found in aquatic birds
- Aquatic birds are natural reservoir for diversity, virus is non-pathogenic for waterfowl
- New combinations of HA and NA as well as the other six genes occur during dual infections, random process
- Certain combinations are successfull, others don't
- Pigs are susceptible to human and avian flu viruses, long thought to be the viral "mixing bowl" from which new human strains emerge
- Swine & poultry often co-located, particularly in Asia

** H5 and H7 inclined to turn highly pathogenic in poultry*

Source: Dr Dave Siegrist, Dr Lynn Cooper, MITRE

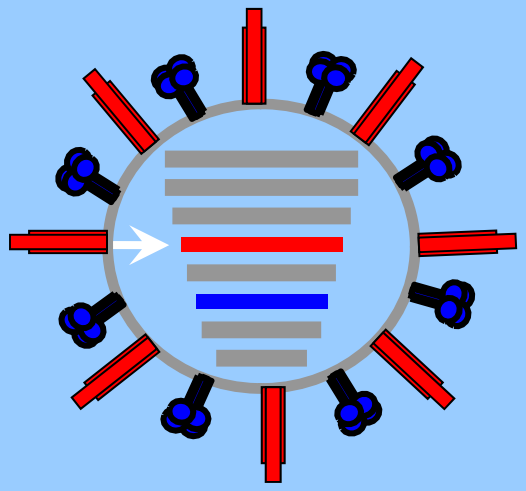
# The Agent: Influenza A & Reassortment

Entry Key Varieties (subtypes)

| | | | |
|---|---|---|---|
| H1 | bird | human | pig |
| H2 | bird | human | |
| H3 | bird | human | pig |
| H4 | bird | | |
| H5 | bird | | |
| ⬇ | | | |
| H16 | bird | | |

H1N1, H3N2 } Seasonal flu

H5N1 Avian flu



Exit Key Varieties (subtypes)

| | | | |
|---|---|---|---|
| N1 | bird | human | pig |
| N2 | bird | human | pig |
| N3 | bird | | |
| ⬇ | | | |
| N9 | bird | | |

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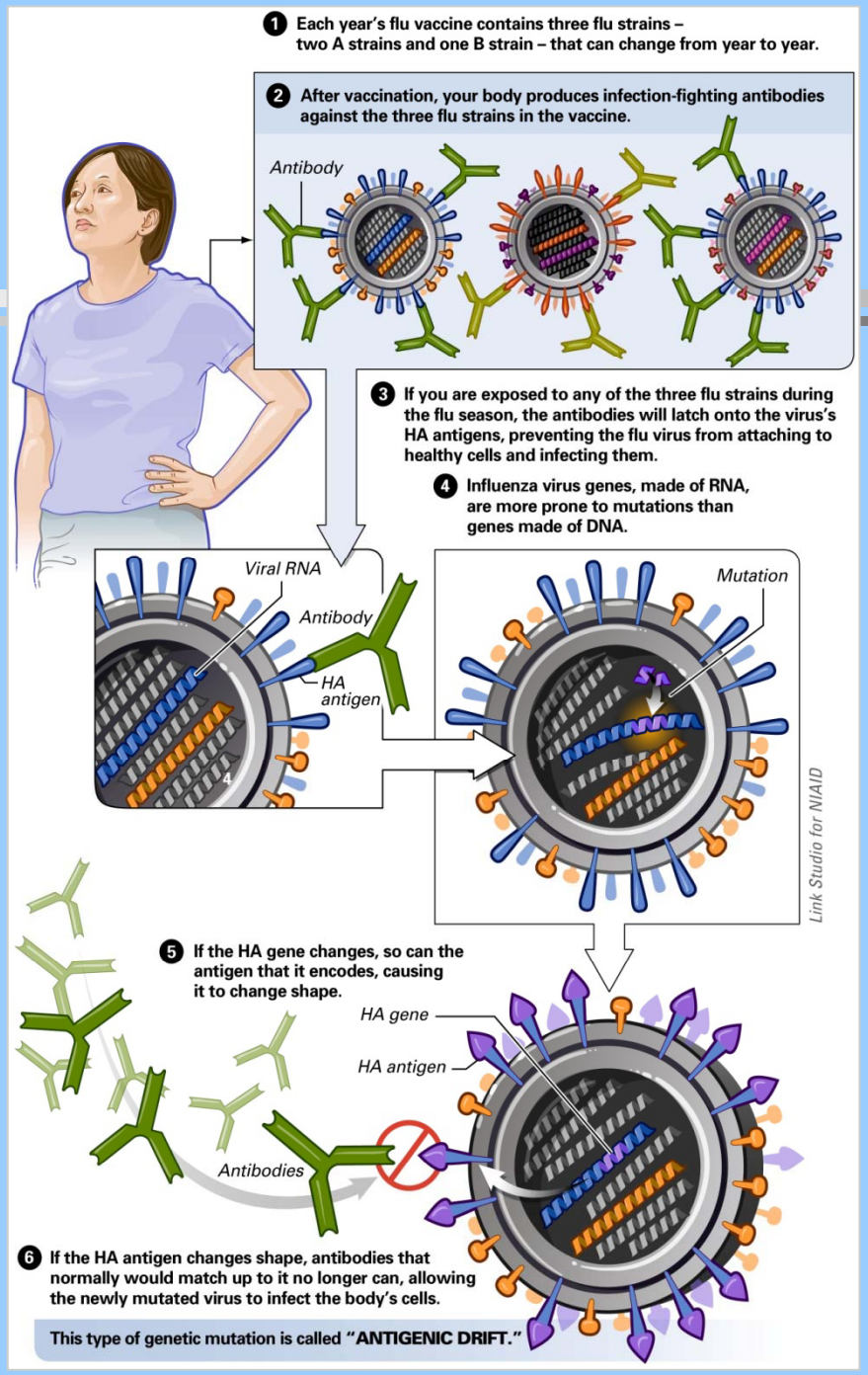
# The Agent: Change Mechanisms

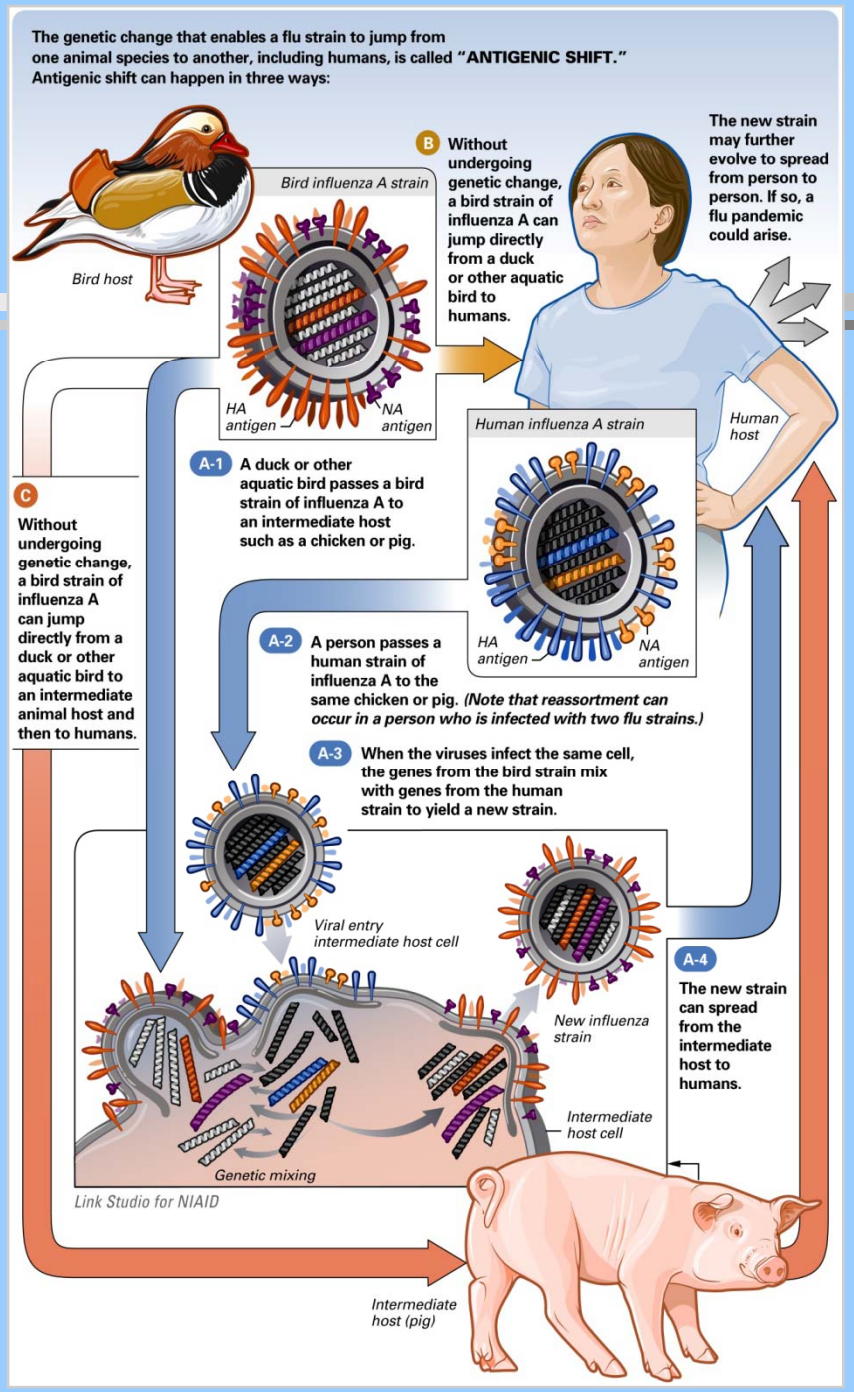
**Antigenic "drift"**

- » Small errors (mutations) occur during the copying of genetic information.
- » Flu A viruses are unable to repair errors.
- » Small changes make the virus look new to the immune system.
- » Immunity against previous strains does not protect against the new version.



# The Agent: Change Mechanisms

- **Antigenic "shift"**
  - » Drastic change in the composition of a virus.
  - » Influenza A viruses can exchange genetic material with other subtypes.
  - » This process results in new combinations of H and N subtypes.
  - » Hong Kong flu resulted from the emergence of a new H3N2 combination.

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# The Agent: Influenza A

Recently Discovered Evidence of a Significant Human/Swine Interaction

Source:  Dr Lynn Cooper, MITRE

# The Agent: The Current H1N1 "Swine" Flu Reassortment Summary

First swine flu virus isolated in 1930 – H1N1 descendant of the 1918 pandemic strain called classical swine viruses

Classical swine flu viruses (H1N1) circulated widely; common in pigs in US, Mexico, Canada, SA, Europe,, Kenya, Mainland China, Taiwan, and Japan

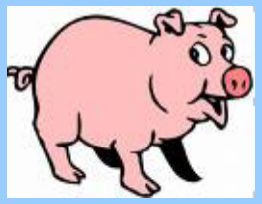
Caused rare human cases ~1 per year; usually associated with underlying chronic condition and/or contact with pigs

Swine are susceptible to human strains, avian strains and swine strains – mixing bowl concept

In late 1990s new triple-reassortant swine strains emerged in US combinations of swine, avian, and human genes: H3N2 with HA, NA, PB1 (human seasonal), PA and PB2 (avian), other 3 genes swine origin; H1N2 triple-reassortants; H1N1 classic swine triple-reassortants

Current H1N1 outbreak strain*:

- HA — H1 swine origin gene of a lineage midway between Eurasian and North American
- NA + M — genes are Eurasian swine new to North America
- PA + PB2 — avian from North American from a triple reassortant swine virus
- PB1 — human seasonal H3N2 from a North American triple reassortant in swine



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* Source: Science Insider, 29 APRIL; interview with Ruben Donis – CDC Atlanta, Dr Dave Siegrist, MITRE

# The Disease: "You and Me"

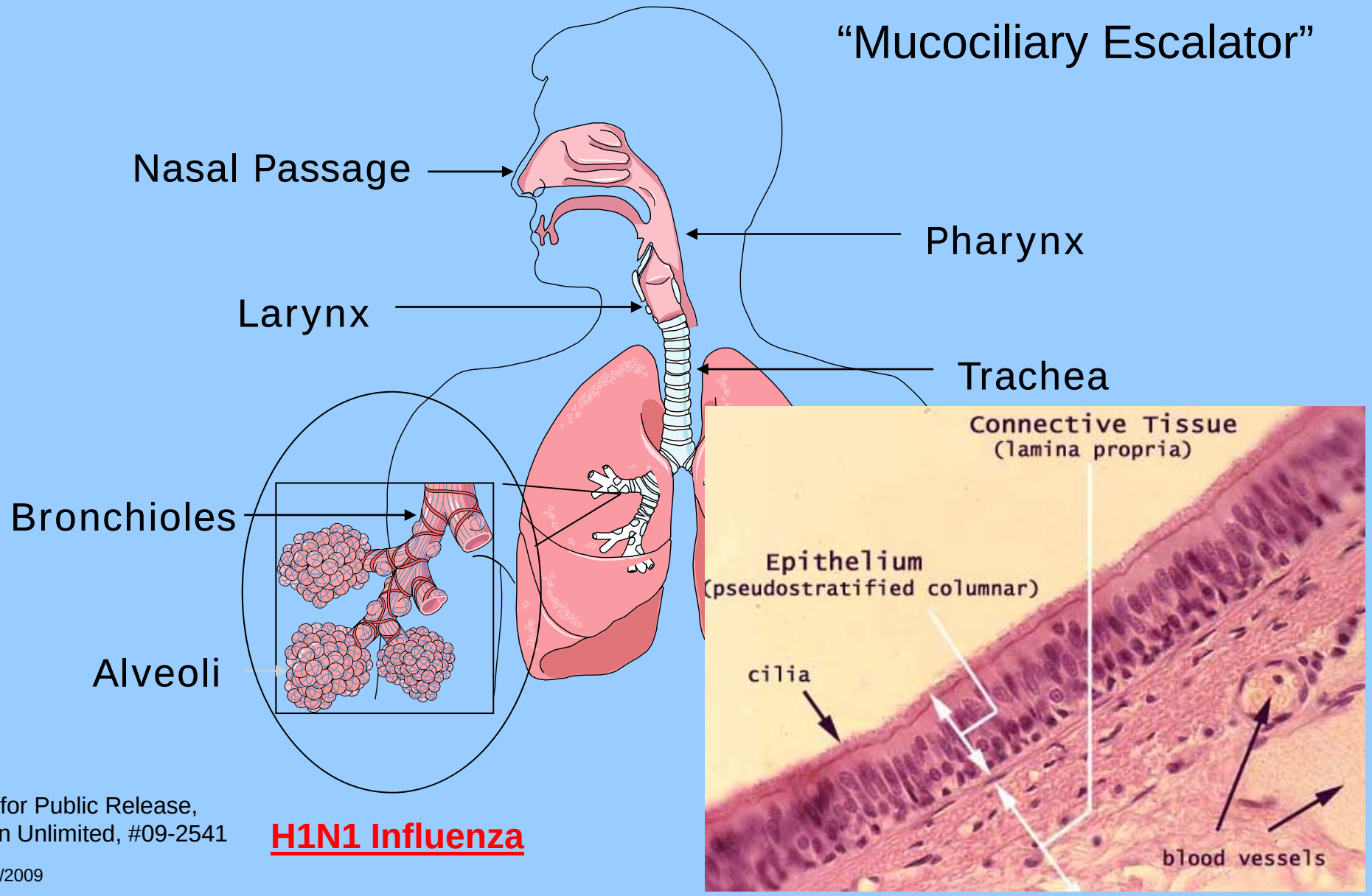
- Who? Where?:  Humans, all ages, anterior nares, nasopharynx
- Modes of Transmission (fomites)
  - » Virus laden droplets in the breathing zone---cough, sneeze
  - » Contaminated Surfaces, Viral Survival: 8-12 hrs (paper), 24-48 hrs (glass), may vary with change in temperature or humidity---touch, cough, sneeze
- Symptoms: sudden onset of high fever, headache, sore throat, non-productive cough, muscle aches, GI upset and fatigue.
- Contagious Period:
  - » Adults—24 hrs prior and up to 7 days post symptoms onset
  - » Children—24 hrs prior and up to 14 days post symptoms onset
- Individual Treatment:
  - » Judicious use of antivirals (Tamiflu—Oseltamivir, Relenza—Zanamivir) x 5 days,  Chemoprophylaxis 5-7 days post exp
  - » Vaccination (if available and appropriate)
  - » Symptomatic Treatment
- Complications can include bacterial pneumonia, dehydration, and worsening of chronic medical conditions.

Influenza germs spread through the air when someone coughs.

Emergency hospital during the 1918 influenza epidemic, Camp Funston, Kansas

# The Disease: “You and Me”

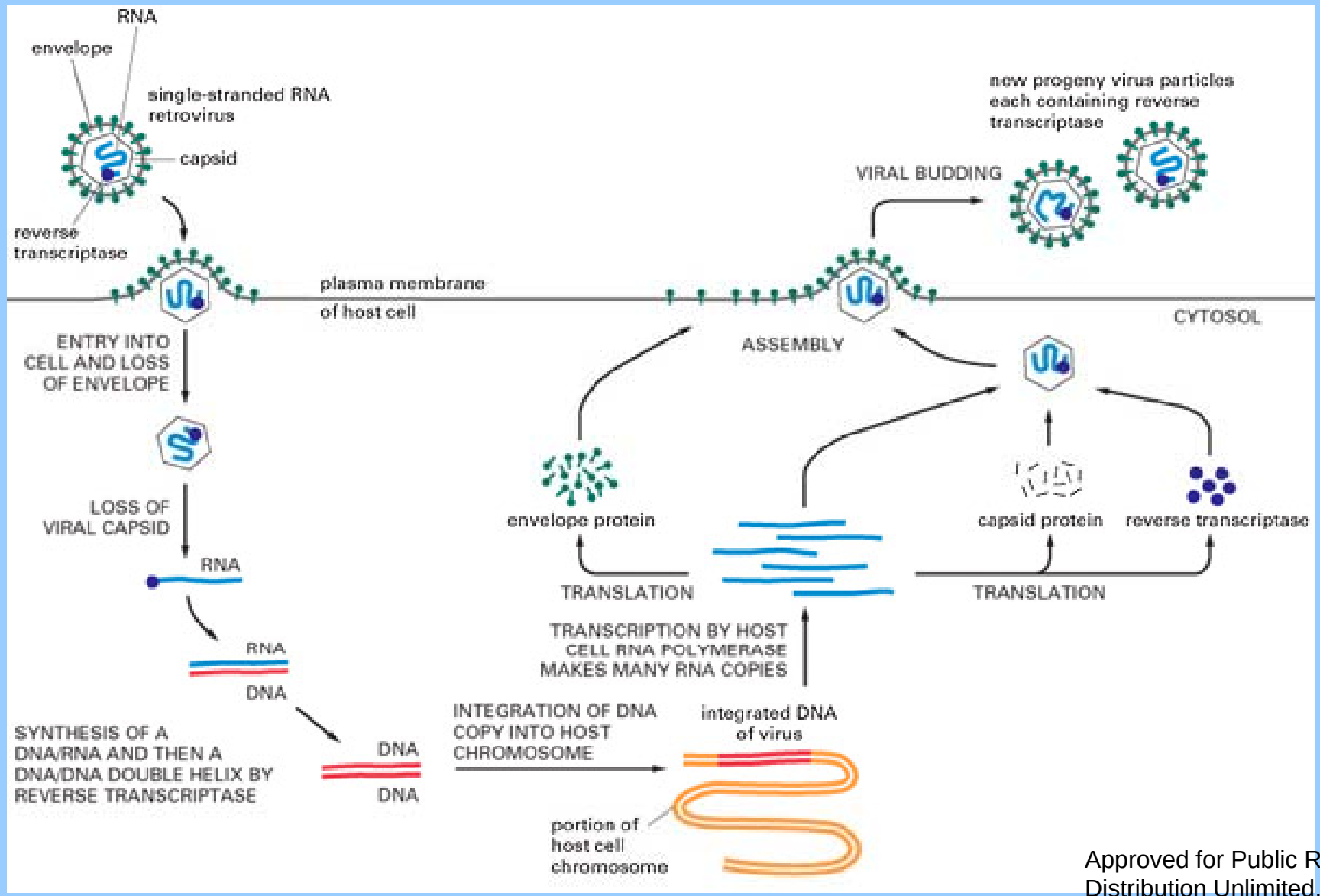
“Mucociliary Escalator”



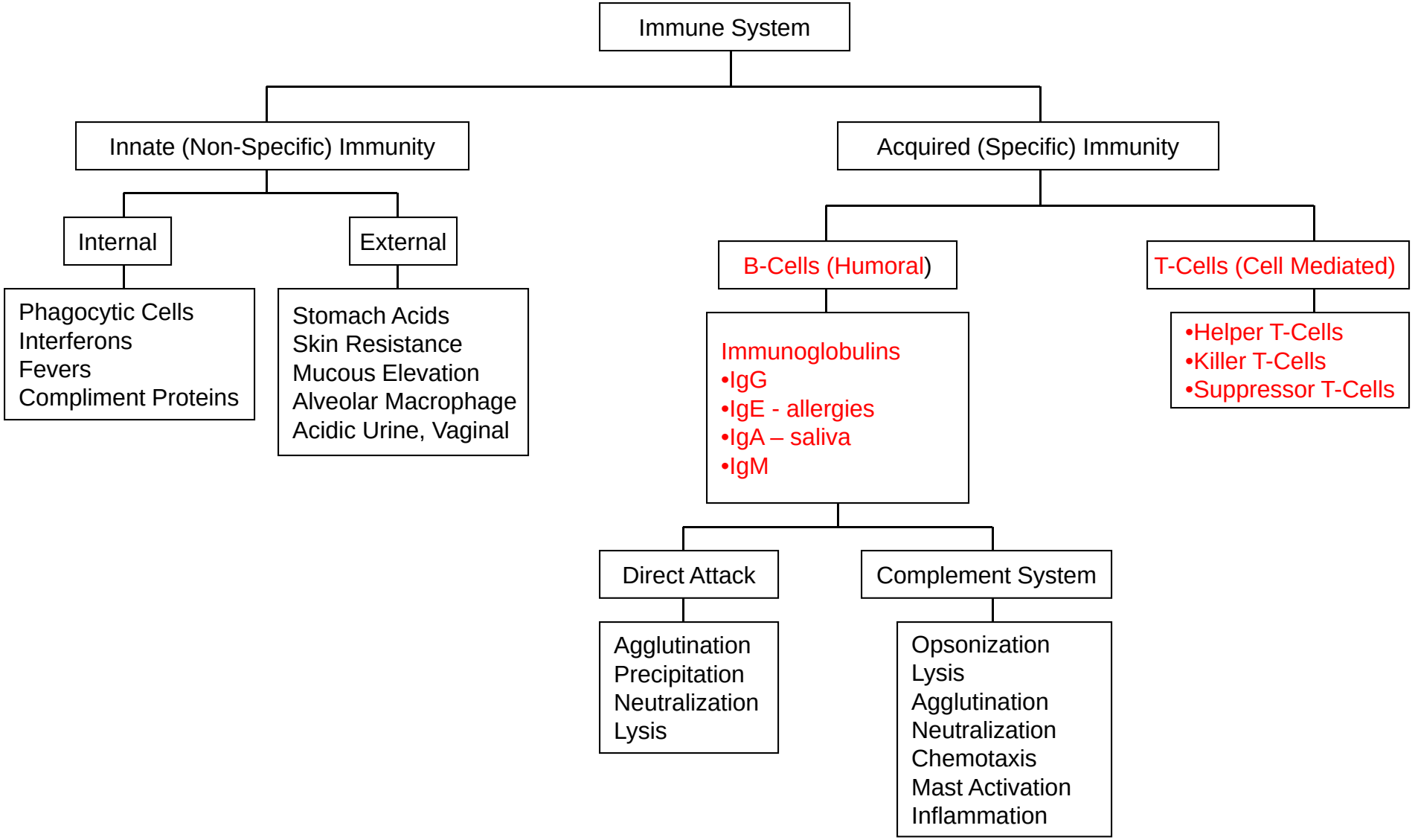



**H1N1 Influenza**

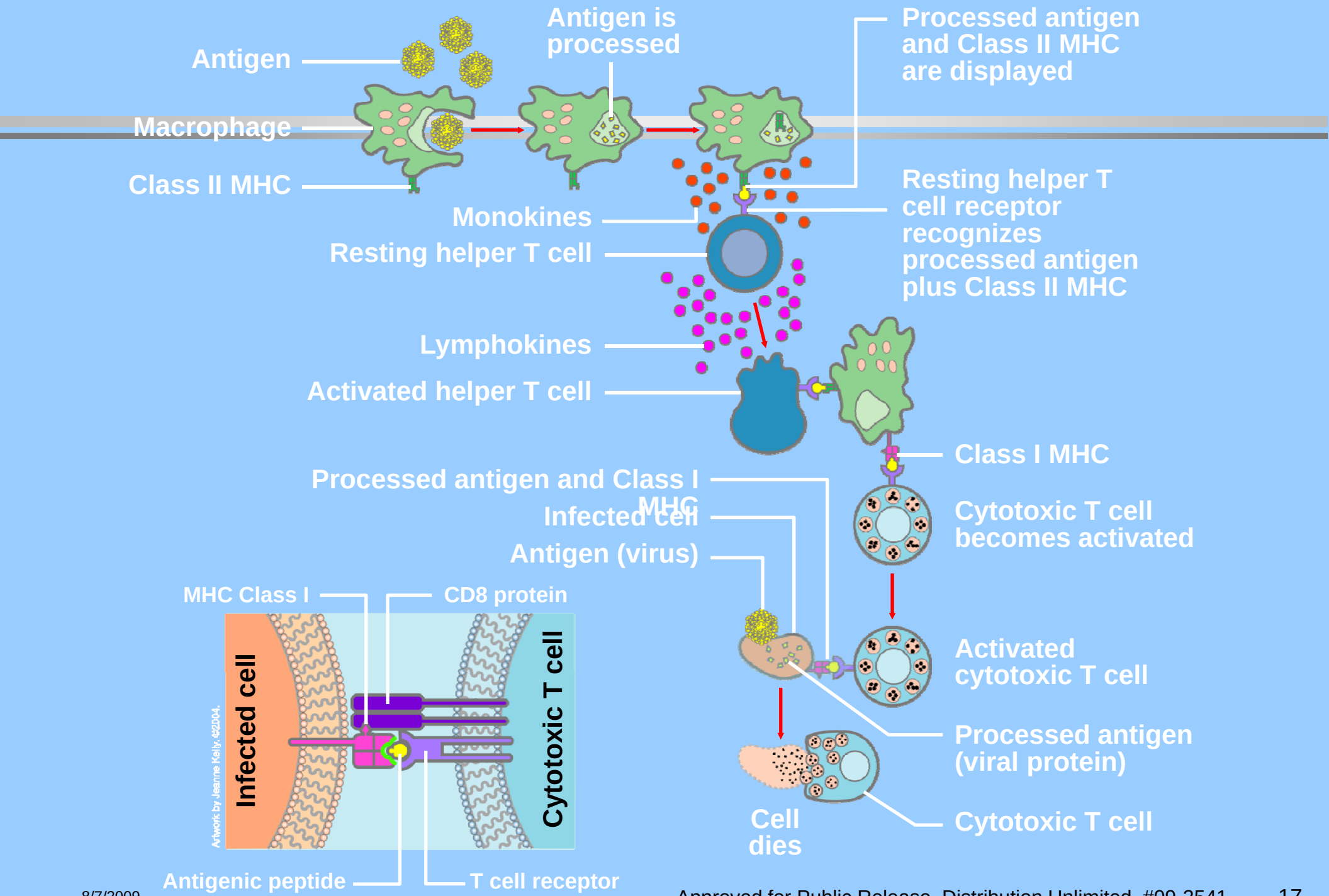
# The Disease: “You and Me”




Respiratory Epithelium



# T-Cell Activation: Cell Mediated Immunity



# The Disease: “You and Me”

## The Immune System Response

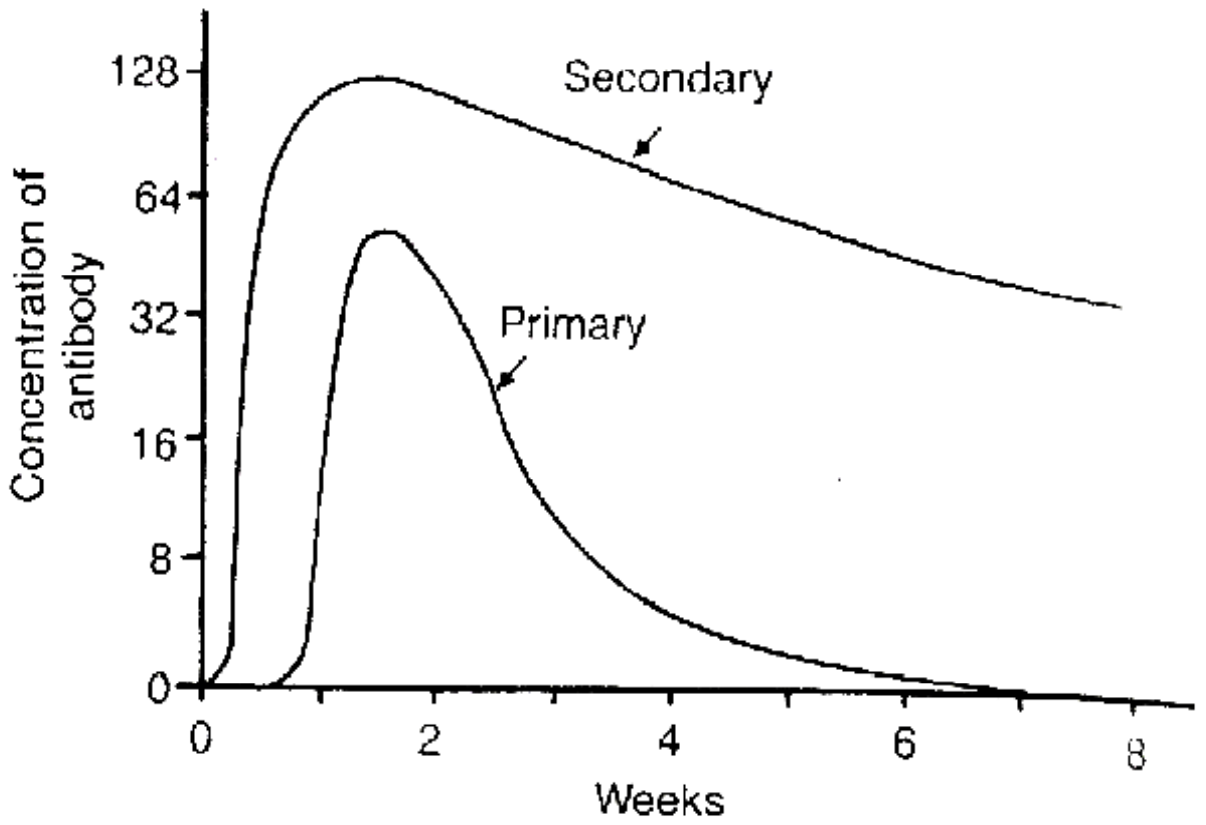
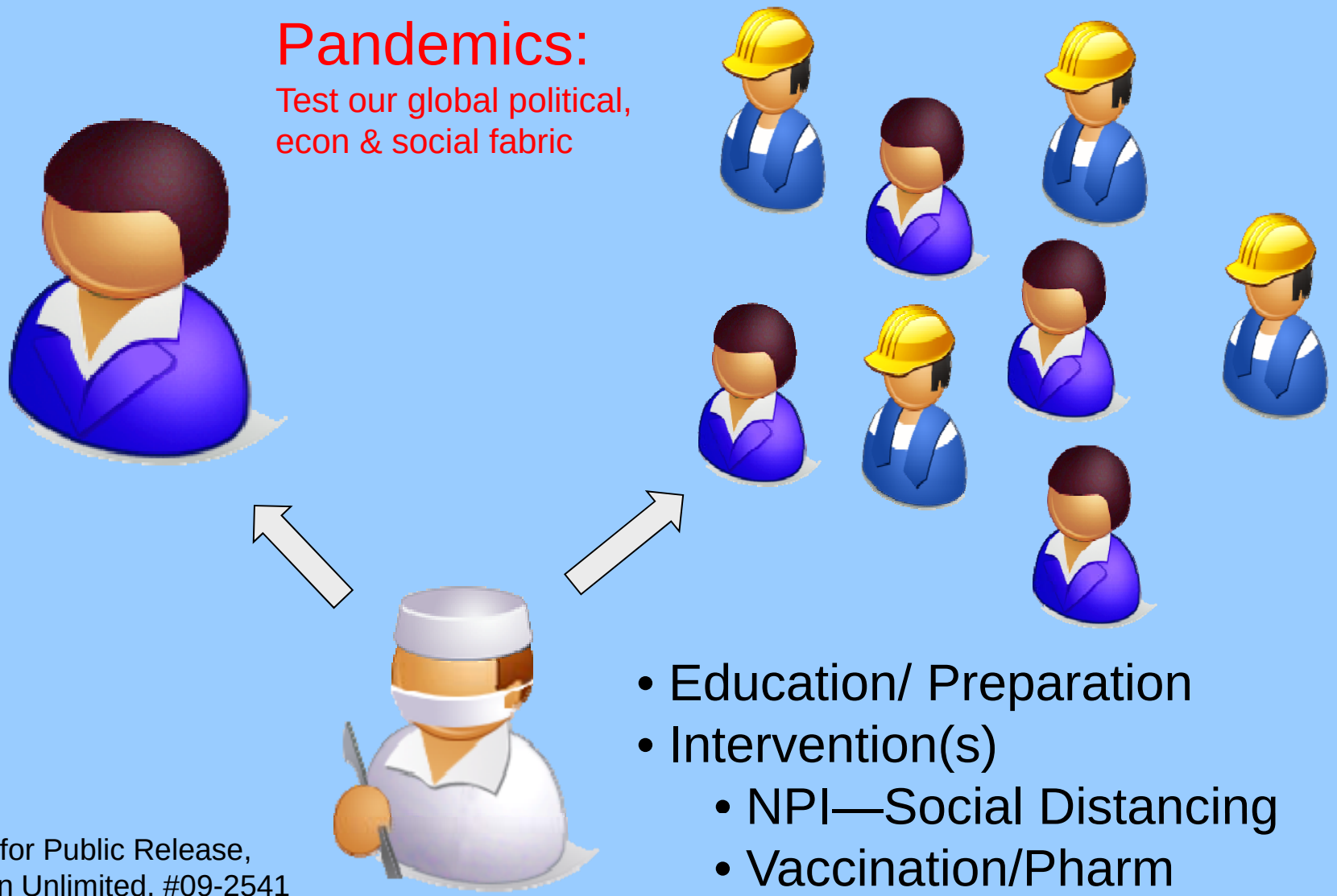



**Figure 34–2.** Time course of the antibody response in the circulating blood to a *primary* injection of antigen and to a *secondary* injection several months later.

# Individuals to Groups (ESE)

## Pandemics:

Test our global political, econ & social fabric

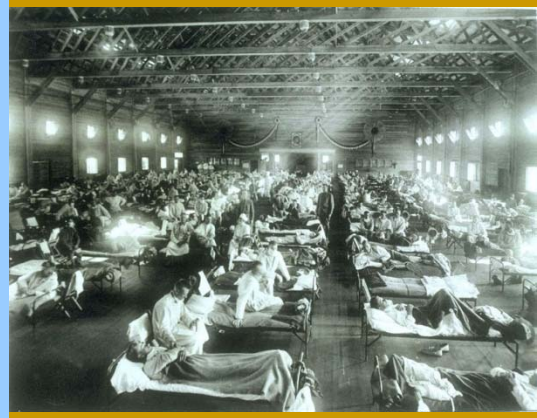


- Education/ Preparation
- Intervention(s)
  - NPI—Social Distancing
  - Vaccination/Pharm
- Communicating/Managing Risk

# The Epidemic: "The Herd" Epidemiologic Terms

- Population Health = Population Resilience
- Epidemiology: "The Study of the distribution and determinants of disease and injuries in human populations"
- Infectious Disease Epidemiology: Host-Parasite Interaction, Mechanisms of Transmission, Type of Epidemic, Epidemic Control Mechanisms
- Agent Assessment: Pathogenicity—Attack Rate, Virulence, CFR, Reservoirs—human/animal
- Epidemic Type: Common Source (John Snow—cholera) vs Propagated (index case, secondary attack rate- "Waves")
- Herd Immunity > 90% immune (vaccinated or previous infection)
- High risk cohorts: elderly, young children, pregnant women, and people with certain health conditions
- Pandemic: A Global Epidemic

Influenza germs spread through the air when someone coughs.



Emergency hospital during the 1918 influenza epidemic, Camp Funston, Kansas

# Global Epidemic = Pandemic

- An influenza pandemic is a global outbreak of disease that occurs when a new influenza A virus appears or "emerges" in the human population, causes serious illness, and then spreads easily from person to person worldwide.
- Pandemics are different from seasonal outbreaks or "epidemics" of influenza. Seasonal outbreaks are caused by subtypes of influenza viruses that are already in existence among people, whereas pandemic outbreaks are caused by new subtypes or by subtypes that have never circulated among people or that have not circulated among people for a long time.
- Past influenza pandemics have led to high levels of illness, death, social disruption, and economic loss.

# Pandemics in 20th Century

1918: "Spanish Flu" 1957: "Asian Flu" 1968: "Hong Kong Flu"

20-40 million deaths 1 million deaths 1 million deaths

H1N1

H2N2

H3N2

1920 1940 1960 1980 2000

# The Next Pandemic: Elevated Risk

Global Scientific,Technical, Social, Political and Economic Issues that put us at increased risk of a PI event:

- New/Novel Strain Appearance (e.g. herd immunity low)
- Difficult Initial Identification (inter mixing of seasonal vs new)
- Increased World Population & Density
- Increased World Travel/Mixing
- Antiviral resistance
- Vaccine Development Technology Limitations (egg vs cell based)
- Traditional Screening Tools (POE's) Less Valuable
- Significant Chronic Disease Population Vulnerability

# Estimates of the Impact of an Influenza Pandemic by Severity [Approx 800 K hospital beds in US, w/ 2/3 staffed]

Quarantine

| | Category 2 (Similar to a 1957 pandemic) | Category 4/5 (Similar to a 1918 pandemic) |
|---|---|---|
| **Illness** | 90 million (30%) | 90 million (30%) |
| **Outpatient medical care** | 45 million (50%) | 45 million (50%) |
| **Hospitalization** | 865,000 | 9, 900,000 |
| **ICU care** | 128,750 | 1,485,000 |
| **Mechanical ventilation** | 64,875 | 745,500 |
| **Deaths** | 209,000 | 1,903,000 |

# Infectious Disease Control/Mitigation Interventions

- Measures directed against the agent reservoir (H1N1, H5N1…)
  - » Culling
  - » Isolation—imposed on individual for maximum incubation period
  - » Quarantine—imposed on groups for maximum incubation period
  - » Social Distancing
- Measures that interrupt the transmission of Organisms
  - » Hospital: Medications—tamiflu, relenza, etc., Universal Precautions & Ventilation Systems--lamilar flow rooms, Infection Control
  - » Community: Medications, PPE/T--N95 Mask, Social Distancing
- Measures to reduce host susceptibility
  - » Vaccination
  - » Intact Immune System
- Disease Surveillance
  - » Screening
  - » Data base analysis and reporting tools
- Historical Probability & Scientific Interconnectedness

# Non-pharmacological Interventions used in the 1918 “Spanish Flu”

- Making influenza a reportable disease
- Isolating sick individuals
- Quarantine of households with sick individuals
- School closure
- Protective sequestration of children or adults
- Cancellation of worship services
- Closure of public gathering places [e.g., saloons, theatres, etc.]
- Staggered business hours to decrease congestion on trams, etc.
- Mandatory or recommended the use of masks in public
- Closing or discouraging the use of public transit systems
- Restrictions on funerals, parties, and weddings
- Restrictions on door-to-door sales
- Community-wide curfew measures and business closures
- Social distancing strategies for those encountering others
- Public health risk communication measures
- Declaration of public health emergency

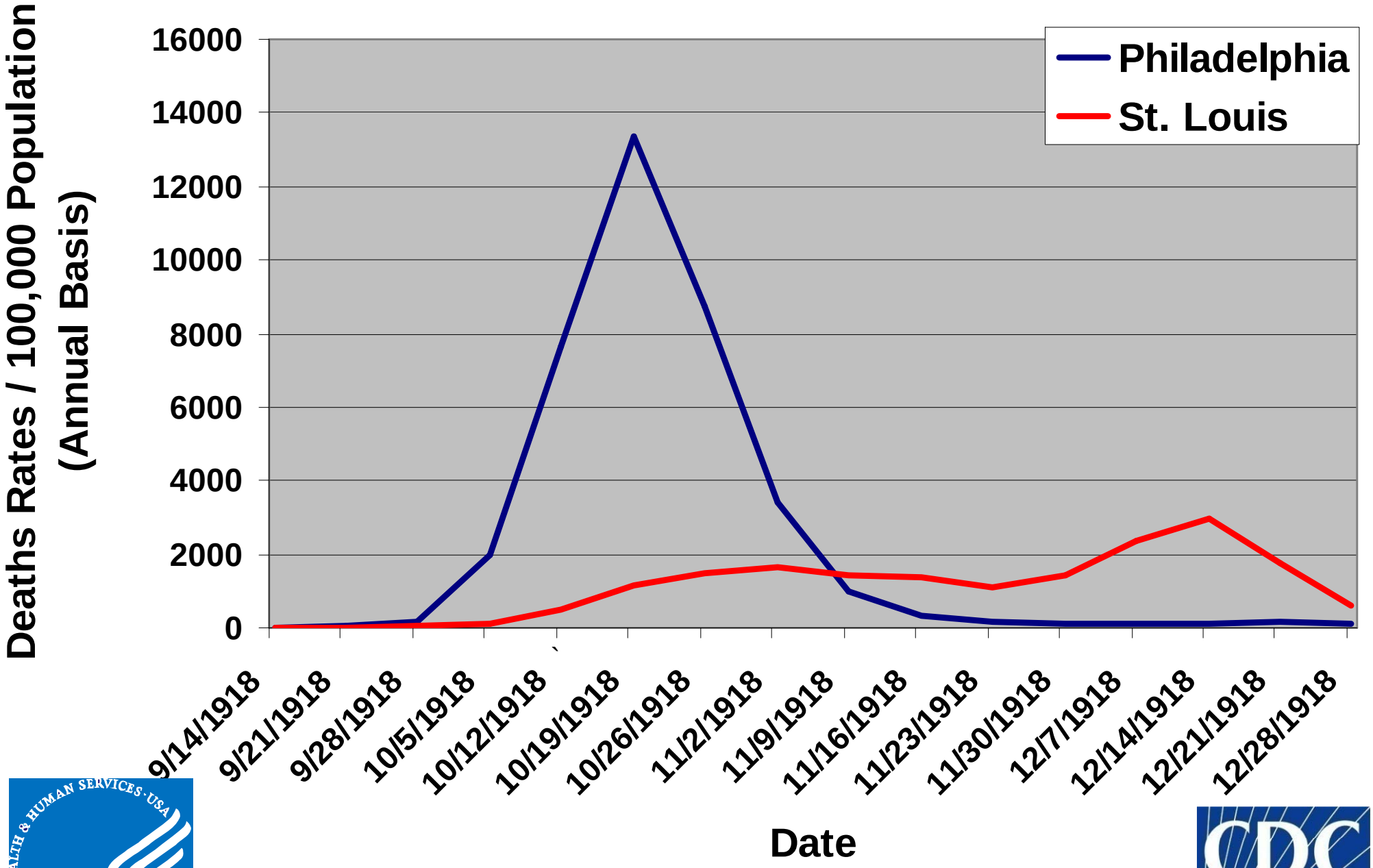
# Historical Data on Non-pharmacological Interventions (NPI)*

- Review of 17 US cities, 1918 pandemic, US
- Cities that implemented *multiple* NPIs *early* in the pandemic, lower death rates
  - » 50% lower peak death rate
  - » 20% lower cumulative death
- Releasing NPIs early resulted in increased death rates

Richard J. Hatchett *, Carter E. Mecher , and Marc Lipsitch.

Public health interventions and epidemic intensity during the 1918 influenza pandemic, PNAS, April 2007

# 1918 Death Rates: Philadelphia v St. Louis



# Who Infects Whom?

Glass, RJ, et al. Local mitigation strategies for pandemic influenza.
NISAC, SAND Number: 2005-7955J

| | To Children | To Teenagers | To Adults | To Seniors | Total From |
|---|---|---|---|---|---|
| **From Children** | 21.4 | 3.0 | 17.4 | 1.6 | 43.4 |
| **From Teenagers** | 2.4 | 10.4 | 8.5 | 0.7 | 21.9 |
| **From Adults** | 4.6 | 3.1 | 22.4 | 1.8 | 31.8 |
| **From Seniors** | 0.2 | 0.1 | 0.8 | 1.7 | 2.8 |
| **Total To** | 28.6 | 16.6 | 49.0 | 5.7 | |

Likely sites of transmission

- School
- Household
- Workplace

Demographics

| | |
|---|---|
| Children/Teens | 29% |
| Adults | 59% |
| Seniors | 12% |

# Communicating Risk

- Technical Expert's definition
  - » Hazard + probability = risk assessment
  - » Relies upon research and statistics
  - » Characterized by health risk assessments
- Public's definition
  - » Consequences of hazards
  - » Individual feelings about likelihood that something bad will happen to them

Risk is about FEAR

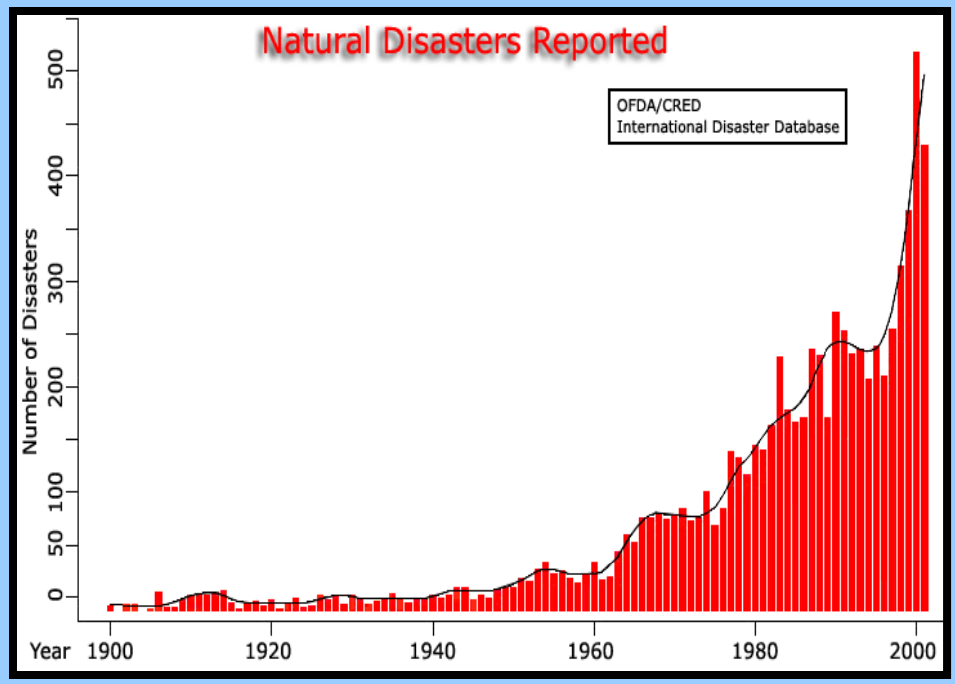
- Public versus Expert "gap"

Risk is about DANGER

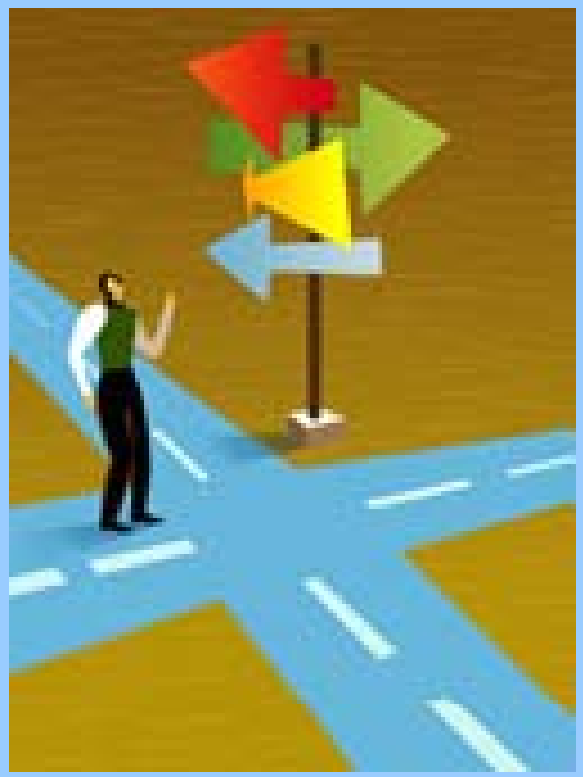
- Emotional
- Contentious

Risk is about SURVIVAL

- Disagreement can be fierce



# OK, so now what doctor?



# Know the Enemy: Differences Between Pandemic Influenza and Seasonal Influenza

- Seasonal Influenza
  - » Occurs in cooler parts of year (winter in USA)
  - » Affects 10% of population
  - » Usually mild and not life threatening
  - » Very young and very old are at highest risk
  - » Vaccine is available and usually protective
  - » Antiviral drugs (Tamiflu, Relenza) are available to treat those few people at special risk

- Pandemic Influenza
  - » Historically pandemics have occurred about every 10-40 years, at any time of year
  - » May affect >50% of population
  - » Illness can be more serious
  - » Cases may come in waves
  - » All age groups at risk
  - » Specific vaccine not yet available, and unlikely to be widely available early in outbreak; may take six months to develop and distribute
  - » Large number of affected people will create large demand; supportive care and potentially limited supply of antiviral drugs

# OK, So now what doctor?

U.S. Army Camp Hospital No. 45, Aix-Les-Bains, France, Influenza Ward No. 1, 1918.

Photo by Dr. Al Jenny

- Stay or Get Informed
  http://www.cdc.gov/h1n1flu/#stay_healthy
- Vaccination
  - » Flu shot or nasal flu spray
  - » Recommended for “at-risk” groups
  - » Given during flu season, starting in October
- Good health habits
  - » Have an N95 Mask available
  - » Wash hands
  - » Avoid touching nose, mouth, and eyes
  - » Cover mouth and nose when coughing or sneezing
  - » Avoid close contact with infected individuals
  - » Avoid public areas when infected
- Develop a family EP&R Plan
  - » Communicate about Finances, Legal, Health
  - » At the “End of the Day”…….

# Questions

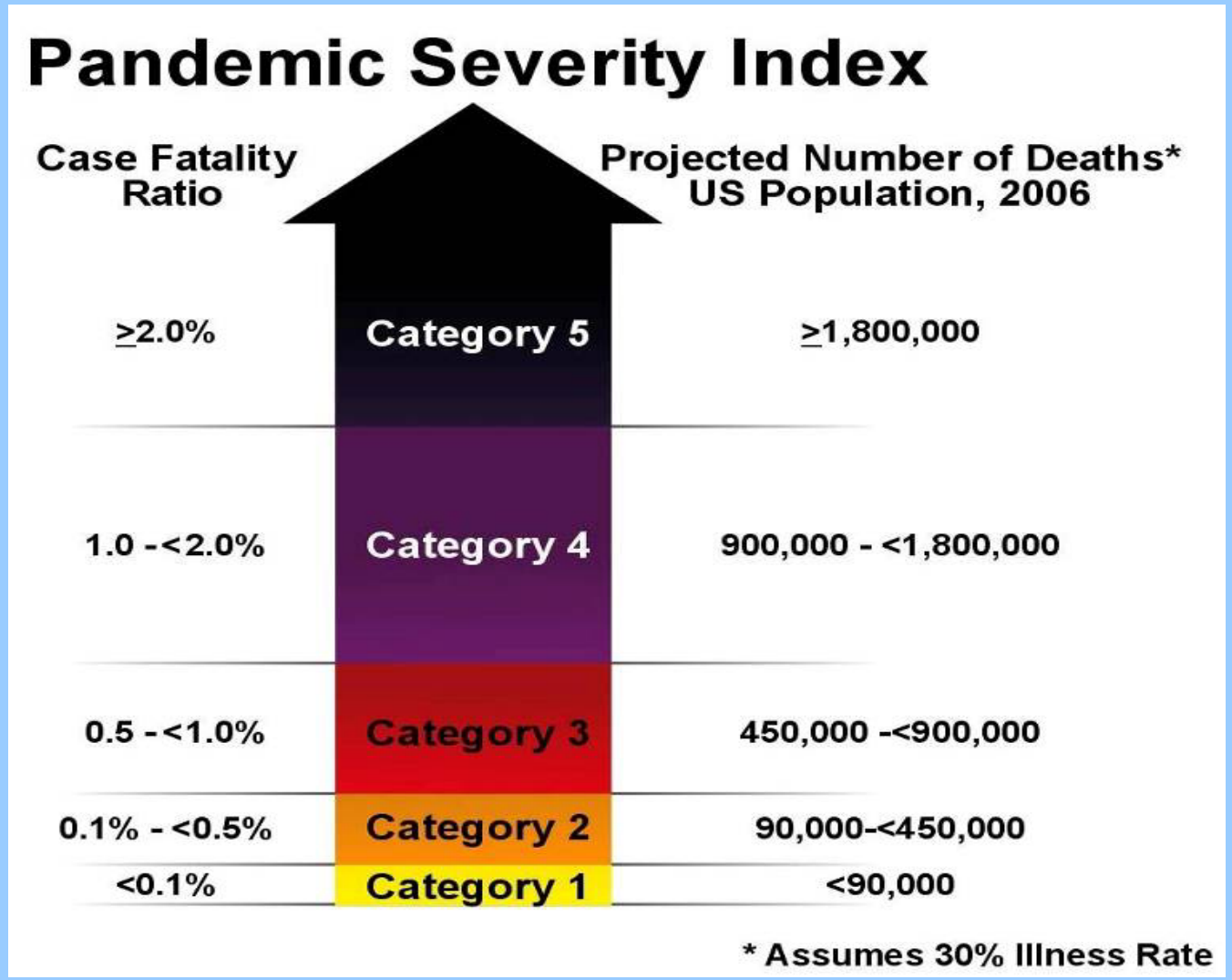
# Definitions

- *Isolation*
  - » Separation of ill persons with contagious diseases
  - » Often in a hospital setting, could be at home
- *Quarantine*
  - » Restriction of persons who are not ill but presumed exposed, usually in the home or a designated facility
- *Social Distancing*

  *"social measures to decrease the frequency of contact among people in order to diminish the risk of spread from communicable diseases"*
- *Infection Control*

  "hygienic measures to decrease spread of infectious pathogens"

# CDC Pandemic Severity Index

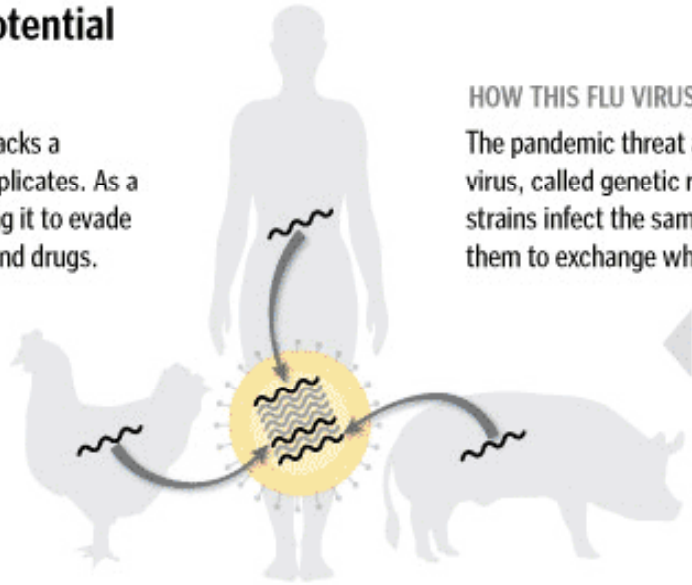


# A Virus With Pandemic Potential

### HOW THE FLU VIRUS MUTATES

The genetic machinery of the flu virus lacks a mechanism to correct errors when it replicates. As a result, it mutates at a high rate, allowing it to evade the body's natural defenses, vaccines and drugs.

**Seasonal flu strains that circulate every winter generally have minor changes** from those of the previous year. But people who have been exposed to flu in the past usually retain a measure of immunity.



### HOW THIS FLU VIRUS IS DIFFERENT

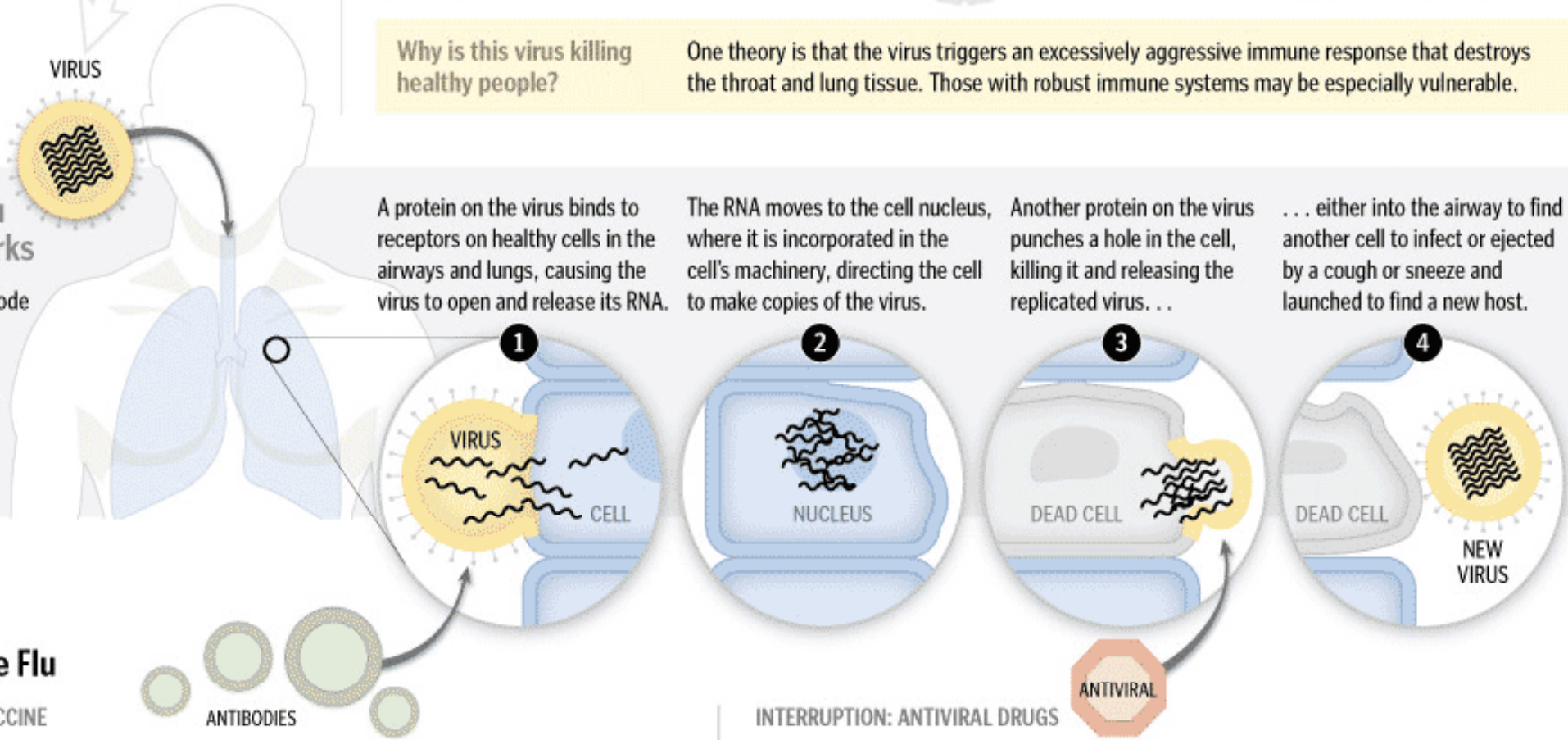
The pandemic threat arises from another trick of the fl virus, called genetic reassortment. When different strains infect the same host at the same time, it allow them to exchange whole sections of their genetic cod

**Scientists think the current virus strain combines genetic material from pigs, birds and humans.** Segments from the three different viruses have created a reassorted virus that has not been seen before.

**Why is this virus killing healthy people?** One theory is that the virus triggers an excessively aggressive immune response that destroys the throat and lung tissue. Those with robust immune systems may be especially vulnerable.

## How a flu virus works

The genetic code of the flu is contained in eight strands of RNA.




## Fighting the Flu

### PREVENTION: VACCINE

Vaccines teach the body's immune system to make antibodies to kill the virus. A weakened form of the virus is grown in hens' eggs, purified and killed with a chemical. Creating a new vaccine takes at least six months and requires hundreds of millions of eggs.

### INTERRUPTION: ANTIVIRAL DRUGS

Relenza and Tamiflu, both shown to be effective against this current virus, stop it from buddin out of the cell if administered soon after symptoms appear. Antivirals can also be given to people in contact with an infected person to prevent the disease from spreading.

# Vaccines,
# from the Washington Post

**Staying the course for now**

Vaccine manufacturers are just beginning production for next winter's regular influenza vaccine, which protects against three human flu strains. Until more is known about the current virus, the World Health Organization said Monday that factories should continue as planned and not change the formula for the seasonal vaccine.

## Time-consuming mission

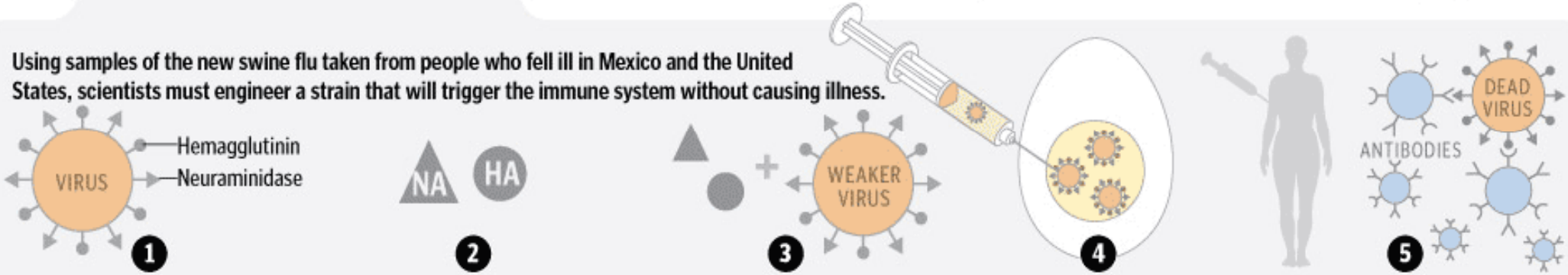
**Creating and distributing a new vaccine typically takes at least 6 months and requires hundreds of millions of eggs.**

The Center for Disease Control and Prevention reported yesterday that scientists have been able to grow the virus in eggs but found the growth to be unusually slow.

It may take several months before any shots are available for the first required safety testing in volunteers.

Then manufacturers would get the strain to start their own production supply, which could take another two months.


**Using samples of the new swine flu taken from people who fell ill in Mexico and the United States, scientists must engineer a strain that will trigger the immune system without causing illness.**




1. The virus carries two proteins on its surface called hemagglutinin (HA) and neuraminidase (NA). HA helps the virus enter healthy cells; NA helps the virus exit cells after it has replicated many times over.

2. These proteins give flu strains their main identity, and scientists must use a technique called **reverse genetics** to match the HA and NA components to form the basis of a vaccine.

3. To create a "seed virus," these components are combined with segments taken from another, weaker flu strain that is known to grow well in hens' eggs.

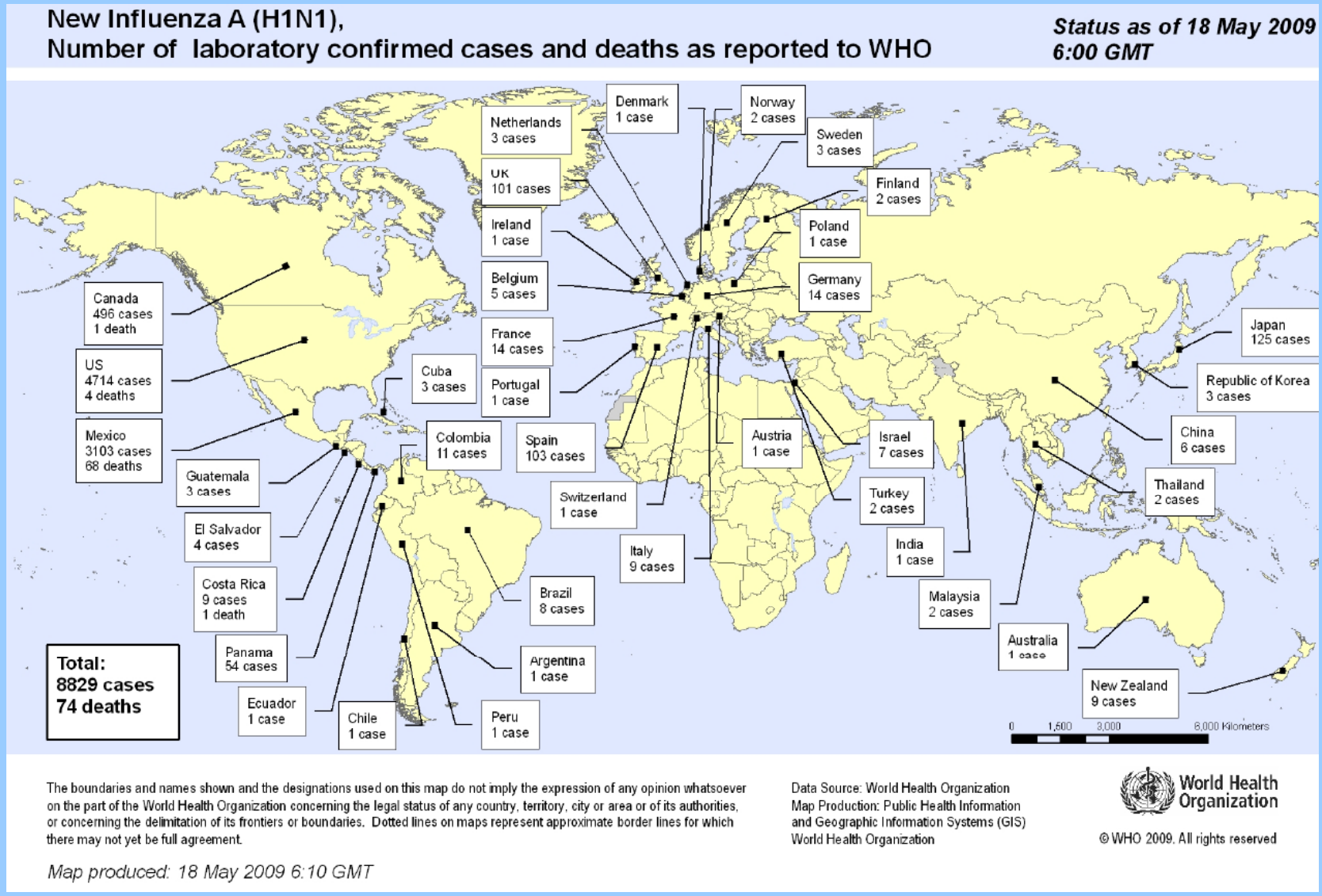
4. The seed virus is inserted into hens' eggs so that it can multiply. From each egg will come one dose of vaccine.

5. The new vaccine is chemically inactivated ("killed") and then injected into humans, prompting the creation of swarms of antibodies that recognize the proteins and can fight the virus.

**Some manufacturers are studying production options.** A cell-based technology* in which viruses are harvested in cell cultures, not eggs, may produce vaccines more rapidly.

*Currently, no cell-based vaccines are approved in the United States.

# WHO Current H1N1 Cases



# Community-Based Interventions

1. Delay disease transmission and outbreak peak
2. Decompress peak burden on healthcare infrastructure
3. Diminish overall cases and health impacts